Citation:

Stott DJ, Falconer A, Kerr GD, Murray HM, Trompet S, Westendorp RG, Buckley B, de Craen AJ, Sattar N, Ford I. Does low to moderate alcohol intake protect against cognitive decline in older people?*J Am Geriatr Soc.* 2008; 56(12): 2,217-2,224.

PubMed ID: 19093921

Study Design:

Prospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To determine whether low to moderate alcohol intake was protective against cognitive decline in older people.

Inclusion Criteria:

5,804 subjects (3,000 women), aged 70-82 years with vascular risk factors or known vascular disease from a randomized placebo-controlled trial of pravastatin.

Exclusion Criteria:

Not described.

Description of Study Protocol:

Recruitment

Subjects were recruited from the Prospective Study of Pravastatin in the Elderly at Risk (PROSPER). The follow-up ended by May 2002.

Design

PROSPER was a randomized placebo-controlled trial of pravastatin. The current study was a prospective cohort study.

Dietary Intake/Dietary Assessment Methodology

Alcohol intake: Assessed at a single time point at study baseline; quantified in terms of usual alcohol intake in units per week for the previous month.

Statistical Analysis

- Female and male non-drinkers: Compared with those with low or moderate amounts of alcohol
- A blinded endpoints committee reviewed and adjudicated all incident vascular endpoints, including all possible strokes and transient ischemic attacks
- Continuous variables (e.g., for triglycerides): Transformed logarithmically to give a near-normal distribution of data for parametric analysis. Statistical significance was set at $P<0.05$.
- Chi-square test: Used for categorical variables
- Analysis of variance: Used for continuous variables
- Baseline associations: Analyzed using general linear models adjusting for covariates
- Longitudinal analyses: Performed using a linear mixed model with the covariates
- Separate analyses: Performed for men and women
- Models with an interaction between time and alcohol intake: Provided an estimate of rate of cognitive decline, expressed as an estimate of the annual change in cognitive function, comparing low and moderate drinkers with non-drinkers as the reference group, adjusting for baseline cognitive function score
- Longitudinal analyses: Performed without this interaction between time and alcohol use
- The linear mixed-model analysis: Allowed for use of all cognitive assessments, including interim measures taken between the baseline and the final assessment
- Analyses: Performed using statistical software SPSS (version 12.0.1, SPSS, Inc., Chicago, IL) and SAS (version 9.1, SAS Institute, Inc., Cary, NC)
- Low alcohol intake: Categorized as 1U to 3U per week for women and 1U to 7U per week for men
- Moderate alcohol intake: Categorized as more than 3U per week for women and more than 7U per week for men.

Data Collection Summary:

Timing of Measurements

- The follow-up was completed by May 2002
- Alcohol intake was assessed at a single time point at study baseline
- Cognitive function was measured at study baseline (mean of two measures taken two weeks apart); nine, 18 and 30 months and at the final trial visit.

Dependent Variables

- Cognitive function:
  - Mini-Mental State Examination (MMSE) was used to assess general cognitive impairment. A cutoff score of 24 points was used as an exclusion criterion to eliminate those with poor cognitive function at baseline
  - Attention and processing speed was assessed using the Stroop Color–Word test and the Letter–Digit Coding Test (LDCT)
  - Memory was tested using the Picture-Word Recall Test (PWRT), which was based on the Groningen Fifteen Words test
- A neuropsychologist and two experienced testers trained all study nurses in test administration for two days or more before the nurses conducted the study assessments. There were annual training sessions and checkup visits at all centers. The tests were administered using explicit guidelines for test administration

- For all analyses, only complete and reliable test results of cognitive function (as indicated by the study nurse who administered the test) were included.

Independent Variables

Alcohol intake: Female and male drinkers were each divided into two equal-sized groups for analysis based on their alcohol intake:

- Women: Cutoff gave 611 (20.4%) defined as having low intake of less than 3U per week and 636 (21.2%) with moderate intake of 3U per week or more
- Men: Cutoff of 7U per week gave 960 (34.2%) defined as having low intake and 1,021 (36.4%) with moderate intake.

Control Variables

- Age
- Country
- Smoking status
- Body mass index (BMI)
- Body weight
- Years of education
- Incident stroke
- History of vascular disease
- Version of test (if applicable).

Description of Actual Data Sample:

- *Initial and final N:* 5,804 subjects (3,000 women)
- *Age:* 70 to 82 years
- *Location:* Community-based study in Ireland, the Netherlands and Scotland.

Summary of Results:

Key Findings

- For females, cognitive performance for all cognitive domains was better for those who drank alcohol vs. non-drinkers over the 3.2-year follow-up
- No significant cognitive performance effects were seen for men (adjusted linear mixed model)
- The rate of cognitive decline was similar for drinkers and non-drinkers for all cognitive domains, except for MMSE, which declined significantly less in female drinkers than non-drinkers (adjusted linear mixed model attenuated rate of decline = 0.05 MMSE units per annum; P=0.001).

Other Findings

- To determine the possibility of attrition bias, linear mixed models with and without time interaction were conducted only for subjects with an MMSE test result in months 36 to 48; 4,599 subjects had a measurement in one of these months
- All significant associations in the original analysis in the female cohort remained significant in this repeat analysis

- For men, the mean difference in MMSE in non-drinkers vs. drinkers across the period of the study became statistically significant; the mean differences over time between the low-intake and non-drinking men and between the moderate-intake and non-drinking men were 0.15 [standard error (SE) = 0.07, P=0.03] and 0.23 (SE=0.07, P=0.001) MMSE units, respectively
- The incidence of non-fatal strokes and transient ischemic attacks (cerebrovascular events) over the course of follow-up was similar across the different categories of alcohol intake for women and men:
  - For women, 106 of 1,753 (6.0%) non-drinkers had a non-fatal cerebrovascular event, compared with 37 of 611 (6.1%) with low alcohol intake and 46 of 636 (7.2%) with moderate intake (chi-square P=0.55)
  - For men, the respective figures were 51 of 823 (6.2%), 73 of 960 (7.6%) and 76 of 1,021 (7.4%) (P=0.46)
- Older age, male sex and lower education were significantly (all P<0.001) associated with poorer cognitive performance.

Author Conclusion:

Low to moderate alcohol consumption might delay age-associated cognitive decline in older women (including slowing decline of global cognitive function), but these effects were not clearly observed in older men.

Reviewer Comments:

- *Drinking habits were recorded only at study baseline, and information on lifetime alcohol consumption was not available*
- *Non-drinkers might have ill health associated with use of medicines that interacted with alcohol. Such ill health may be a confounder and cause impairment of cognitive function in a subgroup of non-drinkers*
- *No information was presented on the type of alcohol consumed*
- *The follow-up time was 3.2 years and only a small decline in cognitive function would be expected*
- *There were likely learning effects in all of the cognitive tests.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes

4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	N/A
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	N/A
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	No

4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	No
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	???
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	Yes
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	No
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	No
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	No
6.6.	Were extra or unplanned treatments described?	No
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A

7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	???
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	N/A
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes